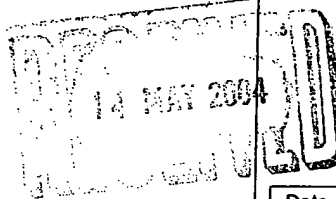


From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

14.5.04  
PCT

To:

Bannerman, David G.  
WITHERS & ROGERS  
Goldings House  
2 Hays Lane  
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GRANDE BRETAGNE



NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing  
(day/month/year)

12.05.2004

Applicant's or agent's file reference  
DGB/KB522PCT

IMPORTANT NOTIFICATION

International application No.  
PCT/EP 03/01304

International filing date (day/month/year)  
10.02.2003

Priority date (day/month/year)  
11.04.2002

Applicant  
KARO BIO AB et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international  
preliminary examining authority:



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
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Authorized Officer

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PCT



INTERNATIONAL PRELIMINARY EXAMINATION REPORT  
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference DGB/KB522PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/01304	International filing date (day/month/year) 10.02.2003	Priority date (day/month/year) 11.04.2002
International Patent Classification (IPC) or both national classification and IPC C07C59/215, C07C59/215		
Applicant KARO BIO AB et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  10.09.2003	Date of completion of this report  12.05.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Pérez Carlon, R  Telephone No. +49 89 2399-8125  

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/01304**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-20 as originally filed

**Claims, Numbers**

1-24 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/01304**

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-24 in part

because:

☒ the said international application, or the said claims Nos. 10-16 and 24 relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-24 in part are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 10, 17

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-24 in part
	No: Claims	
Inventive step (IS)	Yes: Claims	1-24 in part
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-9, 17-23
	No: Claims	

2. Citations and explanations

**see separate sheet**

**Re Item I**

**Basis of the report**

1. The terms on claim 1 "a bioisosteric equivalent" and "a prodrug" do not clearly define the subject-matter for which protection is sought (Art. 6 PCT). This Examination Report has been carried out as if these expressions were not present in the claims.

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. Claims 10-16 and 24 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
2. The expression "a disease... dependent on the expression of a T3 regulated gene..." on claims 10 and 17 does not clearly define the subject-matter for which protection is sought. The search was restricted to the diseases mentioned in their dependent claims.

Claims related to inventions in respect of which no Search Report has been established need not be subject of International Preliminary Examination (Rule 66.1(e) PCT).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

- D1: WO 02 092550 A
- D2: WO 00 39077 A
- D3: WO 99 00353 A
- D4: WO 01 98256 A
- D5: WO 01 60784 A
- D6: WO 01 36365 A

1. The present application refers to compounds of the general formula as in claim 1, their compositions and therapeutical uses.

The compounds of claim 1 differ from *all* the documents of the art in the presence of the **indan moiety**, and:

- the compounds of D1 and D6 contain a -CH<sub>2</sub>-O- group linking the two aromatic rings and not a -O-
- those of D2 posses a H- or acyl group instead of the R<sub>5</sub>-(CH<sub>2</sub>)<sub>n</sub> unit
- for those of D3, R<sub>5</sub>-(CH<sub>2</sub>)- = H
- the compounds of D4 posses a amino/amido group instead of the ether unit R<sub>5</sub>-(CH<sub>2</sub>)-O-.
- in D5, the possibility R<sub>5</sub>-(CH<sub>2</sub>)-O- = Aryloxy is contemplated in the Markush formula, but all the compounds of the examples present R<sub>5</sub>-(CH<sub>2</sub>)-O- = -OH or -OMe.

Claims 1-24 are new in the sense of Art. 33(2) PCT.

2. In light of the state of the art, the problem to be solved by the present application is regarded as to the provision of alternative thyroid receptor ligands.
3. According to the applicant, the compounds of the application present ThR $\alpha$  affinities from 100 to 500 nM. The problem is considered as solved.

No indications have been found that would have led the skilled person to modify the known thyroid receptor ligands in the present way.

An inventive step in the sense of Art. 33(3) PCT is therefore acknowledged.